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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,382	09/09/2004	Jian Luo	MGC020325	6441

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EXAMINER	
DICKINSON, PAUL W	

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1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,382	LUO ET AL.	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7 and 9-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7, and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 3/28/2009, have been fully considered but they are not deemed to be fully persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objects are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Arguments

Claim Rejections - 35 USC § 103

The rejection of claims 1-4, 7, and 9-11 under 35 U.S.C. 103(a) as being unpatentable over Weintraube et al (Atherosclerosis, 1998) is maintained.

Applicant argues the following points:

(1) Gemfibrozil and metformin are used for two very different types of patients. While Weintraube et al teaches that gemfibrozil effectively reduced PPLp in patients with type IV HLP, it fails to teach that metformin may be used in patients with type IV HLP.

(2) Weintraube et al teaches that the two drugs take effect in different time frames with metformin requiring twice as long as gemfibrozil. This difference in time frame is a teaching away from combining the two drugs.

(3) Applicant argues unexpected results, specifically the synergistic effect of adding gemfibrozil and metformin as disclosed in Examples 1 and 2 of the specification.

Applicant's arguments have been fully considered but are not found persuasive for the following reasons:

(1) It is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose. The Examiner maintains that gemfibrozil and metformin are used for the very same purpose, i.e. for the clearance of PPLp. Weintraube teaches that "gemfibrozil... and metformin were shown to be beneficial in the clearance of PPLp…" (see abstract; conclusion). Applicant argues that although the effect is the same, the patient populations are different (gemfibrozil was administered to Type IV HLP patients and metformin was administered to glucose intolerance patients). The Examiner agrees with Applicant, but the reference teaches that what unifies these conditions is that they are all atherogenic conditions (see 4. Discussion). Thus, the patient populations overlap in that they are all patients with atherogenic conditions. One of ordinary skill in the art would therefore take from Weintraube that both compounds may be used for the clearance of PPLp in patients suffering from atherogenic conditions. As the two compounds are used for the very same purpose (i.e. clearance of PPLp in patients suffering from atherogenic conditions), their combination is obvious.

(2) That gemfibrozil and metformin each take affect in different time frames is not a teaching away from their combination. There is nothing contraindicative in combining two drugs that have different affect windows. It would be well within the purview of one of ordinary skill to measure and optimize the affect times of the combined formulation.

(3) Regarding Applicant's claim of unexpected results, Example 1 demonstrates that administering 100 mg/kg of gemfibrozil, 90 mg/kg of metformin, and water to mice once a day for 3 days produces a synergistic reduced plasma glucose concentration. Example 2 demonstrates that administering 2.5 mg/kg ciprofibrate, 90 mg/kg metformin, and water to mice once a day for 4 days produces a synergistic reduced plasma glucose concentration. The problem with the results is that they are not commensurate in scope with the claims, which encompass: (1) any dosage regime of metformin and non-glucose-lowering fibrate, whereas the results are limited to two dosage regimes (100 mg/kg gemfibrozil, 90 mg/kg metformin administered once a day for 3 days and 2.5 mg/kg ciprofirbate, 90 mg/kg metformin, administered once a day for 4 days); (2) any non-glucose-lowering fibrate, whereas the results are limited to two non-glucose-lowering fibrates (gemfibrozil and ciprofibrate); and (3) one or more pharmaceutically acceptable inactive ingredient(s), whereas the results are limited to one pharmaceutically acceptable inactive ingredient (water). Accordingly, Applicant has not demonstrated that the unexpected results would hold over the scope of the claimed invention (with a representative number of dosage regimes, a representative number of non-glucose-lowering fibrates, and a representative number of pharmaceutically acceptable inactive ingredients).

New Grounds of Rejection

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 7, and 9-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The specification and original claims fail to support the presently claimed invention of "A pharmaceutical composition consisting of... a glucose-lowering agent metformin... and...a lipid-improving agent selected from non-glucose-lowering fibrates... *in combination with one or more pharmaceutically acceptable inactive ingredients*." :Pharmaceutically acceptable inactive ingredients" is vague and indefinite (see ***Claim Rejections - 35 USC § 112, Second Paragraph*** below) but may reasonably be considered a subset of "pharmaceutically acceptable ingredients". Although the as-filed application supports "pharmaceutically acceptable ingredients", it does not support the narrower concept of "pharmaceutically acceptable inactive ingredients". The only pharmaceutically acceptable ingredient disclosed is water, and this compound is not necessarily an inactive ingredient (see rejection below). There is no disclosure of a representative number of examples or the concept of "pharmaceutically acceptable inactive ingredients" in the specification or as filed claims. Therefore, the skilled practitioner would not believe that Applicant had possession of the invention at the time of filing.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 7, and 9-11 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "pharmaceutically acceptable inactive ingredients" renders the claims indefinite. This phrase is not a term of art nor is it defined in the specification. It is unclear what ingredients are encompassed by this term for the following two reasons:

(1) It is unclear if this phrase is meant to mean ingredients that are pharmaceutically acceptable and also inactive, or ingredients that are pharmaceutically acceptable and pharmaceutically inactive. In other words, does "pharmaceutically" modify both "acceptable" and "inactive", or "acceptable" only?

(2) If the phrase is interpreted to mean "pharmaceutically inactive", it is unclear in what way these ingredients are "pharmaceutically inactive". Does this mean that the ingredient does not give a pharmaceutical effect (of any kind)? Does this mean that the ingredient does not play a role in the specific chemistry of the metformin and lipid-improving agent selected from non-glucose-lowering fibrates? Does this mean that the ingredient does not play any role (chemical or otherwise) in biological processes? The only example of a pharmaceutically acceptable ingredient for use in the invention is water. In Examples 1 and 2, water is co-administered with the metformin and lipid-improving agent selected from non-glucose-lowering fibrates. However, water is not an

inactive ingredient, as it is an active and vital component in nearly all biological chemistry, and may even be considered a drug, in that it is used to treat dehydration.

For the reasons above, the skilled practitioner would not know the scope of "pharmaceutically acceptable inactive ingredients" nor would they know when they are infringing on the claimed invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

May 26, 2009